Complete Summary

GUIDELINE TITLE

Thrombocytopenia.

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2005 Apr 17 [Various].

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Vilpo J. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 11 [various].

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On January 6, 2006, Cangene, Baxter Healthcare and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revisions to the WARNINGS, PRECAUTIONS and ADVERSE REACTIONS sections of the prescribing information for WinRho SDF (Rho[D] Immune Globulin Intravenous [Human]) to address two important safety concerns.

1. Postmarketing safety surveillance has shown rare, but severe and sometimes fatal, intravascular hemolysis and potentially serious complications, including disseminated intravascular coagulation in patients with ITP.
2. Maltose in IVIG products, such as the liquid formulation of WinRho SDF, has been shown to give falsely high blood glucose levels in certain types of blood glucose testing systems. Due to the potential for falsely elevated glucose readings, only testing systems that are glucose-specific should be used to test or monitor blood glucose levels in patients receiving this product.

See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Thrombocytopenia

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Hematology
Internal Medicine
Pediatrics

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Adults and children with thrombocytopenia

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Assessment of causes of thrombocytopenia
2. Laboratory studies, as indicated, such as haemoglobin, leucocyte count and differential, platelet count and bone marrow examination, platelet antibody assessment, measurement of platelet life-span with radioactively labelled platelets
3. Manual check of platelets when a low count has been detected by automatic counter

Treatment/Management

1. Avoidance of or stopping possible thrombocytopenia-causing drugs
2. Monitoring of symptomless patients
3. Referral, as indicated, to a specialist (in internal medicine or haematology)
4. Hospitalization, if symptoms of bleeding
5. Pharmacologic treatment of idiopathic thrombocytopenia (ITP) (corticosteroids, including predniso[lo]ne [corticosteroid use is controversial among paediatric haemotologists]; intravenous gamma globulin infusions; other drugs, including immunosuppressants and fibrinolysis inhibitors)
6. Splenectomy
7. Transfusions
8. Oprelvekin

MAJOR OUTCOMES CONSIDERED

- Incidence of drug-induced thrombocytopenia
- Need for platelet transfusion in chemotherapy-induced thrombocytopenia
- Platelet count and platelet recovery
- Adverse effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
C. Limited research-based evidence. At least one adequate scientific study.
D. No research-based evidence. Expert panel evaluation of other information.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Clinical Approach

- Remember the possibility of so-called pseudothrombocytopenia.
- Stop drugs possibly causing thrombocytopenia unless vitally indicated.
- If the thrombocytopenic patient has symptoms of bleeding, immediate hospitalization is advisable.

Basic Rules

- The pathophysiological mechanism of thrombocytopenia (blood platelet count $<150 \times 10^9$/L, in late pregnancy $< 120 \times 10^9$/L) may be
    - Decreased production in the bone marrow
    - Increased peripheral consumption
    - Increased sequestration in the spleen
- Artificially low platelet counts are occasionally obtained when counted from ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood (pseudothrombocytopenia). When thrombocytopenia ($<100 \times 10^9$/L) is detected in a patient for the first time, the same blood sample should be checked manually for the presence of thrombocyte aggregates.
- Thrombocytopenia is only a symptom, the cause of which should be clarified. Typical manifestations of thrombocytopenia are skin bruising and petechiae and mucous membrane bleeding. In particular, gum and nasal bleeding is common. Bleeding may also take place in the gastrointestinal and urinary tracts. Menorrhagia is also common.
- A tendency towards bleeding is uncommon if the platelet count is 50 to 100 x 10^9/L. Platelet concentrations of 10 to 50 x 10^9/L are frequently associated with spontaneous bleeding, and haemorrhages are often severe with platelet counts of $<10 \times 10^9$/L.

Causes of Thrombocytopenia

Decreased Production

- Inborn causes
    - Pancytopenias and thrombocytopenias
    - Bone marrow infiltrates
    - Rubella
    - Maternal use of thiazide diuretics during pregnancy
- Acquired causes
    - Aplastic anaemia
    - Bone marrow infiltrates (carcinoma, leukaemia, myelofibrosis, myelodysplasia, tuberculosis)
    - Ionizing radiation, other causes of myelosuppression
    - Drugs (trimethoprim-sulfamethoxazole, gold, thiazide diuretics, alcohol, oestrogens, interferons)
    - Deficiency of vitamins and other essential trace elements or nutrients (B_{12}, folate, iron)
    - Viral infections (in Henoch-Schonlein purpura, the thrombocyte count is normal)
    - Uraemia
    - Heavy drinking
    - Pregnancy

Increased Consumption

- Inborn causes
    - Non-immunological (haemolytic disease of the newborn, prematurity, maternal pre-eclampsia, renal vein thrombosis, infections)
    - Immunological (drug-induced, isoimmune neonatal thrombocytopenia, maternal idiopathic thrombocytopenia purpura [ITP])
- Acquired causes
    - Non-immunological (infections, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, haemolytic-uraemic syndrome, drug-induced over-consumption of platelets)
    - Immunological (drug-induced, in connection with anaphylaxis, following blood transfusion, chronic and acute ITP) (see the Finnish Medical Society Duodecim guideline: "Bruises and purpura in children: ITP and its differential diagnosis")

Platelet Sequestration

- Hypersplenism and hypothermia

Loss of Platelets

- Haemorrhage and haemoperfusion

Clinical Approach

Symptomless Patient, Platelet Count 100–150 x 10^9/L

- The general practitioner can safely follow the situation, initially at intervals of a few months. If no underlying disease becomes evident and thrombocytopenia remains stable, no further follow-up is required. All drugs causing thrombocytopenia should be avoided if possible.
- Many drugs cause thrombocytopenia relatively frequently (George et al., 1998; The Database of Abstracts of Reviews of Effectiveness [DARE]-989740, 2000) [C]. These include heparin, quinidine, chloroquine, gold, salicylates, sulphonamides, thiazides, allopurinol, phenytoin, carbamazepine, and trimethoprim. Non-steroidal anti-inflammatory drugs (NSAIDs) (especially acetylsalicylic acid) and some other medicines (clopidogrel) frequently impair platelet function and bring about a bleeding tendency. This tendency is disproportionately strong among thrombocytopenic patients. Paracetamol appears not to impair platelet function.

Symptomless Patient, Platelet Count <100 x 10^9/L

- Thrombocytopenia-causing drugs should be stopped. Basic investigations are performed: haemoglobin, leucocyte count and differential, platelet count, and bone marrow examination.
- If the situation does not improve, referral to a specialist in internal medicine or haematology is advisable.
- If there are no obvious reasons for thrombocytopenia, platelet antibody assessment should be carried out early.

- Sometimes it is necessary to measure platelet life-span with radioactively labeled platelets. This investigation gives information about the kinetic nature (poor platelet production or decreased survival) of thrombocytopenia.
- Pseudothrombocytopenia: thrombocytes are aggregated in an EDTA tube.

If a Thrombocytopenia Patient Has Symptoms of Bleeding

- He/she needs specialist care.
- It is important to detect the possible cause. Remember that the list of drugs possibly causing thrombocytopenia is very long. All these drugs should be avoided.

Idiopathic Thrombocytopenic Purpura (ITP)

- Treatment is planned by a specialist in internal medicine, a paediatrician, or haematologist.
- In adults, predniso(lo)ne continues to be the first-line therapy. The starting dose is 1 to 2 mg/kg/day. Response to treatment is often achieved in 1 to 4 weeks. At least a partial response is observed in 70 to 90% of cases, but a good one (i.e., platelet count >100 x 10^9/L) in only 30 to 50% of the patients. After a maximal response is observed, the drug is slowly (over weeks) tapered to the smallest dose resulting in an acceptable clinical situation, say a platelet count >50 x 10^9/L, with no symptoms of bleeding. Among paediatric haematologists the use of corticosteroids in ITP has been more controversial, because spontaneous remissions are very frequent (see the Finnish Medical Society Duodecim guideline: "Bruises and purpura in children: ITP and its differential diagnosis").
- Intravenous gamma globulin infusions may induce a response faster than corticosteroids. Non-responders are treated with immunosuppressants or splenectomy.
- Fibrinolysis inhibitors may be used to reduce excessive mucous membrane haemorrhages, such as nasal, gastrointestinal, and urinary tract bleeding and menorrhagia. Platelet transfusions are effective if no platelet antibodies are present. Massive bleeding is compensated with red cells, fresh-frozen plasma, and platelet concentrates.

Related Evidence

- Oprelvekin may accelerate platelet recovery and reduces the need for platelet transfusion in chemotherapy-induced thrombocytopenia (Wilde & Faulds, 1998; DARE-981457, 2001) [C].

Definitions:

Levels of Evidence

A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
C. Limited research-based evidence. At least one adequate scientific study.

D. No research-based evidence. Expert panel evaluation of other information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Effective evaluation and management of thrombocytopenia

POTENTIAL HARMS

- Artificially low platelet counts are occasionally obtained when counted from ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood using automatic counters (pseudothrombocytopenia).
- In a systematic review, the most frequent adverse effects of oprelvekin were oedema and dyspnoea.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Apr 30 (revised 2005 April 17)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Juhani Vilpo

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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This guideline updates a previous version: Vilpo J. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 11 [various].

GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer as of February 7, 2003. The summary was updated by ECRI on April 2, 2004, on October 5, 2004, and June 28, 2005. This summary was updated by ECRI on January 31, 2006, following release of a public health advisory from the U.S. Food and Drug Administration regarding the use of WinRho SDF (Rho(D) Immune Globulin Intravenous [Human]).

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